

WHAT IS CLAIMED IS:

1. A method for treating a patient comprising administering a humanized Class III, anti-CEA, monoclonal antibody (mAb) to said patient in an effective amount for treatment.
2. The method of claim 1, wherein the constant regions of said mAb are from a human IgG1 antibody.
3. The method of claim 1, wherein said mAb comprises a complementarity-determining region (CDR) selected from the group consisting of KASQDVGTSVA (SEQ ID NO:20), WTSTRHT (SEQ ID NO:21), QQYSLYRS (SEQ ID NO:22), TYWMS (SEQ ID NO:23), EIHPDSSTINYAPSLKD (SEQ ID NO:24), LYFGFPWFAY (SEQ ID NO:25), and a combination thereof, wherein said mAb is unreactive with meconium antigen by enzyme immunoassay.
4. The method of claim 3, wherein said mAb retains the binding specificity of a parental murine Class III, anti-CEA mAb which comprises said CDRs.
5. The method of claim 1, wherein said treatment comprises administering said mAb to patients with a CEA-producing cancer.
6. The method of claim 5, wherein said CEA-producing cancer is selected from the group consisting of colon cancer, breast cancer and lung cancer.
7. The method of claim 1, wherein said mAb further comprises framework regions (FRs) of light and heavy chain variable regions from a human antibody.
8. The method of claim 1, wherein said mAb further comprises framework regions (FRs) in the light and heavy chain variable regions, wherein each FR is separately a FR of a human antibody.
9. The method of claim 8, wherein each of said light and heavy chain variable regions chains comprise FRs from at least two human antibodies.

10. The method of claim 7, wherein the light chain variable region comprises a framework region (FR) selected from the group consisting of DIQLTQSPSSLSASVGDRVITTC (SEQ ID NO:26); WYQQKPGKAPKLLIY (SEQ ID NO:27); GVP(S or D)RFSGS(G or V) SGTDFTFITSSSLQPEDIATYYC (SEQ ID NO:28); FGQGTKVEIK (SEQ ID NO:29) or a combination thereof; and the heavy chain variable region comprises a framework region (FR) selected from the group consisting of EVQLVESGGGVVQPG RSLRLSCSSSGFDFT (SEQ ID NO:30), EVQLVESGGGVVQPG RSLRLSCSASGFDFT (SEQ ID NO:31); WVRQAPGKGLEWVA (SEQ ID NO:33); RFTIS RDNSKNTLFLQMDSL RPEDTGVYFCAS (SEQ ID NO:36), RFTISRDN AKNTLFLQMDSL RPEDTGVYFCAS (SEQ ID NO:37); WGQGTPVTVSS (SEQ ID NO:39); and a combination thereof; and wherein C may be in the sulfhydryl or disulfide form.

11. The method of claim 10, wherein the light chain and heavy chain variable regions comprise FRs comprising:

FRL1 comprises DIQLTQSPSSLSASVGDRVITTC (SEQ ID NO:26);

FRL2 comprises WYQQKPGKAPKLLIY (SEQ ID NO:27);

FRL3 comprises GVP(S or D)RFSGS(G or V) SGTDFTFITSSSLQPEDIATYYC (SEQ ID NO:28);

FRL4 comprises FGQGTKVEIK (SEQ ID NO:29);

FRH1 comprises EVQLVESGGGVVQPG RSLRLSCSSSGFDFT (SEQ ID NO:30), or EVQLVESGGGVVQPG RSLRLSCSASGFDFT (SEQ ID NO:31);

FRH2 comprises WVRQAPGKGLEWVA (SEQ ID NO:33);

FRH3 comprises RFTIS RDNSKNTLFLQMDSL RPEDTGVYFCAS (SEQ ID NO:36), or RFTISRDN AKNTLFLQMDSL RPEDTGVYFCAS (SEQ ID NO:37); and

FRH4 comprises WGQGTPVTVSS (SEQ ID NO:39);

and wherein C may be in the sulfhydryl or disulfide form.

12. A method for treating a patient comprising administering a conjugate to said patient in an effective amount for treatment, wherein said conjugate comprises:

a therapeutic agent bound to a humanized Class III, anti-CEA, monoclonal antibody (mAb) or a fragment thereof, wherein said mAb or fragment thereof comprises a complementarity-determining region (CDR) selected from the group consisting of

KASQDVGTSVA (SEQ ID NO:20), WTSTRHT (SEQ ID NO:21), QQYSLYRS (SEQ ID NO:22), TYWMS (SEQ ID NO:23), EIHPDSSTINYAPSLKD (SEQ ID NO:24), LYFGFPWFAY (SEQ ID NO:25), and a combination thereof, wherein said mAb is unreactive with meconium antigen by enzyme immunoassay.

13. The method of claim 12, wherein said mAb retains the binding specificity of a parental murine Class III, anti-CEA mAb which comprises said CDRs.

14. The method of claim 12, wherein said therapeutic agent comprises a cytotoxic agent or an immunomodulator.

15. The method of claim 14, wherein said cytotoxic agent comprises doxorubicin, methotrexate, taxol, ricin A or a radionuclide.

16. The method of claim 15, wherein said radionuclide comprises ^{131}I .

17. The method of claim 12, further comprising administering a second therapeutic agent to said patient.

18. The method of claim 17, wherein said second therapeutic agent is doxorubicin, methotrexate, taxol, ricin A, or a radionuclide.

19. The method of claim 14, wherein said cytotoxic agent is a radionuclide, and said method further comprises administering a second therapeutic agent or performing a treatment regimen to said patient.

20. The method of claim 19, wherein said treatment regimen is a bone marrow reinfusion.

21. The method of claim 19, wherein said radionuclide is ^{131}I .

22. The method of claim 12, wherein said mAb retains the binding specificity of a parental murine Class III, anti-CEA mAb which comprises said CDRs.

23. The method of claim 12, wherein said treatment comprises administering said conjugate to a patient with a CEA-producing cancer.

24. The method of claim 23, wherein said CEA-producing cancer is selected from the group consisting of colon cancer, breast cancer and lung cancer.

25. The method of claim 12, said mAb or fragment thereof further comprises framework regions (FRs) of light and heavy chain variable regions from a human antibody.

26. The method of claim 12, wherein said mAb further comprises framework regions (FRs) in the light and heavy chain variable regions, wherein each FR is separately a FR of a human antibody.

27. The method of claim 26, wherein each of said light and heavy chain variable regions chains comprise FRs from at least two human antibodies.

28. The method of claim 25, wherein the light chain variable region comprises a framework region (FR) selected from the group consisting of DIQLTQSPSSLSASVGDRVITTC (SEQ ID NO:26); WYQQKPGKAPKLLIY (SEQ ID NO:27); GVP(S or D)RFSGS(G or V) SGTDFTFITSSLPEDIATYYC (SEQ ID NO:28); FGQGTKVEIK (SEQ ID NO:29) and a combination thereof; and the heavy chain variable region comprises a framework region (FR) selected from the group consisting of EVQLVESGGGVVQPG RSLRLSCSSSGFDFT (SEQ ID NO:30), EVQLVESGGGVVQPGRSLRLSCSASGFDFT (SEQ ID NO:31); WVRQAPGKGLEWVA (SEQ ID NO:33); RFTIS RDNSKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:36), RFTISRDNAKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:37); WGQGTPVTVSS (SEQ ID NO:39); and a combination thereof; and wherein C may be in the sulfhydryl or disulfide form.

29. The method of claim 28, wherein the light chain and heavy chain variable regions comprise FRs comprising:

FRL1 comprises DIQLTQSPSSLSASVGDRVITTC (SEQ ID NO:26);

FRL2 comprises WYQQKPGKAPKLLIY (SEQ ID NO:27);

FRL3 comprises GVP(S or D)RFSGS(G or V) SGTDFTFITISLQPEDIATYYC (SEQ ID NO:28);
 FRL4 comprises FGQGTKVEIK (SEQ ID NO:29);
 FRH1 comprises EVQLVESGGGVVQPG RSLRLSCSSSGFDFT (SEQ ID NO:30), or
 EVQLVESGGG VVQPGRSLRLSCSASGFDFT (SEQ ID NO:31);
 FRH2 comprises WVRQAPGKGLEWVA (SEQ ID NO:33);
 FRH3 comprises RFTIS RDNSKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:36), or
 RFTISRDNAKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:37); and
 FRH4 comprises WGQGTPVTVSS (SEQ ID NO:39);
 and wherein C may be in the sulfhydryl or disulfide form.

30. A method for diagnosing a patient comprising administering a conjugate to said patient in an effective amount for diagnosis, wherein said conjugate comprises:
 a diagnostic agent bound to a humanized Class III, anti-CEA, monoclonal antibody (mAb) or a fragment thereof, wherein said mAb or fragment thereof comprises a complementarity-determining region (CDR) selected from the group consisting of KASQDVGTSA (SEQ ID NO:20), WTSTRHT (SEQ ID NO:21), QQYSLYRS (SEQ ID NO:22), TYWMS (SEQ ID NO:23), EIHPDSSTINYAPSLKD (SEQ ID NO:24), LYFGFPWFAY (SEQ ID NO:25), and a combination thereof, wherein said mAb is unreactive with meconium antigen by enzyme immunoassay.

31. The method of claim 30, wherein said mAb retains the binding specificity of a parental murine Class III, anti-CEA mAb which comprises said CDRs.

32. The method of claim 30, wherein said diagnostic agent comprises an imaging agent.

33. The method of claim 32, wherein said imaging agent is a radionuclide or a metal chelator complexed radionuclide.

34. The method of claim 33, wherein said radionuclide is iodine, yttrium or technetium.

35. The method of claim 34, wherein said radionuclide is ¹³¹I.

36. The method of claim 30, wherein said diagnosis comprises administering said conjugate to a patient with a CEA-producing cancer.

37. The method of claim 36, wherein said CEA-producing cancer is selected from the group consisting of colon cancer, breast cancer and lung cancer.

38. The method of claim 30, said mAb or fragment thereof further comprises framework regions (FRs) of light and heavy chain variable regions from a human antibody.

39. The method of claim 30, wherein said mAb further comprises framework regions (FRs) in the light and heavy chain variable regions, wherein each FR is separately a FR of a human antibody.

40. The method of claim 39, wherein each of said light and heavy chain variable regions chains comprise FRs from at least two human antibodies.

41. The method of claim 38, wherein the light chain variable region comprises a framework region (FR) selected from the group consisting of DIQLTQSPSSLSASVGDRVITC (SEQ ID NO:26); WYQQKPGKAPKLLIY (SEQ ID NO:27); GVP(S or D)RFSGS(G or V) SGTDFTFITSSLPEDIATYYC (SEQ ID NO:28); FGQGTKVEIK (SEQ ID NO:29) and a combination thereof; and the heavy chain variable region comprises a framework region (FR) selected from the group consisting of EVQLVESGGGVVQPG RSLRLSCSSSGFDFT (SEQ ID NO:30), EVQLVESGGGVVQPGRSLRLSCSASGFDFT (SEQ ID NO:31); WVRQAPGKGLEWVA (SEQ ID NO:33); RFTIS RDNSKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:36), RFTISRDNAKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:37); WGQGTPVTVSS (SEQ ID NO:39); and a combination thereof; and wherein C may be in the sulfhydryl or disulfide form.

42. The method of claim 41, wherein the light chain and heavy chain variable regions comprise FRs comprising:

FRL1 comprises DIQLTQSPSSLSASVGDRVITC (SEQ ID NO:26);

FRL2 comprises WYQQKPGKAPKLLIY (SEQ ID NO:27);

FRL3 comprises GVP(S or D)RFSGS(G or V) SGTDFTFITISLQPEDIATYYC (SEQ ID NO:28);

FRL4 comprises FGQGTKVEIK (SEQ ID NO:29);

FRH1 comprises EVQLVESGGGVVQPG RSLRLSCSSSGFDFT (SEQ ID NO:30), or
EVQLVESGGG VVQPGRSLRLSCSASGFDFT (SEQ ID NO:31);

FRH2 comprises WVRQAPGKGLEWVA (SEQ ID NO:33);

FRH3 comprises RFTIS RDNSKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:36), or
RFTISRDNAKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:37); and

FRH4 comprises WGQGTPVTVSS (SEQ ID NO:39);

and wherein C may be in the sulfhydryl or disulfide form.

43. A Class III, anti-CEA monoclonal antibody (mAb) or antigen-binding fragment thereof comprising a complementarity-determining region (CDR) selected from the group consisting of KASQDVGTSVA (SEQ ID NO:20), WTSTRHT (SEQ ID NO:21), QQYSLYRS (SEQ ID NO:22), TYWMS (SEQ ID NO:23), EIHPDSSTINYAPSLKD (SEQ ID NO:24), LYFGFPWFAY (SEQ ID NO:25), and a combination thereof, wherein said mAb is unreactive with meconium antigen by enzyme immunoassay.

44. The mAb or fragment thereof of claim 43, wherein said mAb retains the binding specificity of a parental murine Class III, anti-CEA mAb which comprises said CDRs.

45. The mAb or fragment thereof of claim 44, wherein the light chain variable region of said mAb or fragment thereof comprises CDRL1 comprising KASQDVGTSVA (SEQ ID NO:20), CDRL2 comprising WTSTRHT (SEQ ID NO:21), and CDRL3 comprising QQYSLYRS (SEQ ID NO:22), and the heavy chain variable region of said mAb or fragment thereof comprises CDRH1 comprising TYWMS (SEQ ID NO:23), CDRH2 comprising EIHPDSSTINYAPSLKD (SEQ ID NO:24) and CDRH3 comprising LYFGFPWFAY (SEQ ID NO:25).

46. The mAb of claim 45, said mAb or fragment thereof is a humanized Class III, anti-CEA mAb and further comprises framework regions (FRs) of light and heavy chain variable regions from a human antibody.

47. The mAb of claim 46, wherein:

(a) the light chain variable regions are characterized by the formula:
FRL1-CDRL1-FRL2-CDRL2-FRL3-CDRL3-FRL4,
wherein each FR is a different framework region of a human antibody, and
FRL1 comprises a region of about 23 amino acids that occurs naturally in the FRL1 of a human antibody;
FRL2 comprises a region of about 15 amino acids that occurs naturally in the FRL2 of a human antibody;
FRL3 comprises a region of about 32 amino acids that occurs naturally in the FRL3 of a human antibody;
FRL4 comprises a region of about 10 amino acids that occurs naturally in the FRL4 of a human antibody; and

(b) the heavy chain variable regions are characterized by the formula:
FRH1-CDRH1-FRH2-CDRH2-FRH3-CDRH3-FRH4,
wherein each FR is a different framework region of a human antibody, and
FRH1 comprises a region of 28-32 amino acids that occurs naturally in the FRH1 of a human antibody;
FRH2 comprises a region of 12-16 amino acids that occurs naturally in the FRH2 of a human antibody;
FRH3 comprises a region of 30-34 amino acids that occurs naturally in the FRH3 of a human antibody; and
FRH4 comprises a region of 9-13 amino acids that occurs naturally in the FRH4 of a human antibody.

48. The mAb of claim 47, wherein

FRL1 comprises DIQLTQSPSSLSASVGDRVITTC (SEQ ID NO:26);
FRL2 comprises WYQQKPGKAPKLLIY (SEQ ID NO:27);
FRL3 comprises GVP(S or D)RFSGS(G or V)SGTDFTFTISSLQPEDIATYYC (SEQ ID NO:28);
FRL4 comprises FGQGTKVEIK (SEQ ID NO:29);
FRH1 comprises EVQLVESGGG VQPGRSLRLSCSSSGFDFT (SEQ ID NO:30), or
EVQLVESGGGVVQPGRSLRLSCSASGFDFT (SEQ ID NO:31);
FRH2 comprises WVRQAPGKGLEWVA (SEQ ID NO:33);
FRH3 comprises RFTISRDN SKNTLFLQMDSL RPEDTGVYFCAS (SEQ ID NO:36), or

RFTISRDNAKNTLFLQMDSLRLPEDTGVYFC AS (SEQ ID NO:37); and
FRH4 comprises WGQGTPVTVSS (SEQ ID NO:39);
and wherein C may be in the sulfhydryl or disulfide form.

49. A humanized Class III, anti-CEA mAb comprising framework regions (FRs) of light and heavy chain variable regions from a human antibody, wherein the light chain variable region comprises a framework region (FR) selected from the group consisting of DIQLTQSPSSLSASVGDRVITC (SEQ ID NO:26); WYQQKPGKAPKLLIY (SEQ ID NO:27); GVP(S or D)RFSGS(G or V) SGTDFTFITISLQPEDIATYYC (SEQ ID NO:28); FGQGTKVEIK (SEQ ID NO:29) and a combination thereof; and the heavy chain variable region comprises a framework region (FR) selected from the group consisting of EVQLVESGGGVVQPG RSLRLSCSSSGFDFT (SEQ ID NO:30), EVQLVESGGG VVQPGRSLRLSCSASGFDFT (SEQ ID NO:31); WVRQAPGKGLEWVA (SEQ ID NO:33); RFTIS RDNSKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:36), RFTISRDNAKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:37); WGQGTPVTVSS (SEQ ID NO:39); and a combination thereof; and
wherein C may be in the sulfhydryl or disulfide form; and
wherein said mAb is unreactive with meconium antigen by enzyme immunoassay and unreactive with normal tissue.

50. The mAb of claim 49, wherein the light chain and heavy chain variable regions comprise FRs comprising:
FRL1 comprises DIQLTQSPSSLSASVGDRVITC (SEQ ID NO:26);
FRL2 comprises WYQQKPGKAPKLLIY (SEQ ID NO:27);
FRL3 comprises GVP(S or D)RFSGS(G or V) SGTDFTFITISLQPEDIATYYC (SEQ ID NO:28);
FRL4 comprises FGQGTKVEIK (SEQ ID NO:29);
FRH1 comprises EVQLVESGGGVVQPG RSLRLSCSSSGFDFT (SEQ ID NO:30), or EVQLVESGGG VVQPGRSLRLSCSASGFDFT (SEQ ID NO:31);
FRH2 comprises WVRQAPGKGLEWVA (SEQ ID NO:33);
FRH3 comprises RFTIS RDNSKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:36), or RFTISRDNAKNTLFLQMDSLRLPEDTGVYFCAS (SEQ ID NO:37); and
FRH4 comprises WGQGTPVTVSS (SEQ ID NO:39);
and wherein C may be in the sulfhydryl or disulfide form.

51. An isolated polynucleotide comprising a nucleic acid sequence encoding the mAb or fragment thereof of claim 43.

52. An expression vector comprising the isolated polynucleotide of claim 51.

53. A transformed cell comprising the isolated polynucleotide of claim 51.

54. The transformed cell of claim 53, wherein said cell is a mammalian cell.

55. A method of producing a Class III, anti-CEA mAb comprising
(a) transforming a cell with the isolated polynucleotide of claim 51; and
(b) expressing said polynucleotide by culturing said cell; and
(c) producing said mAb.

56. A complementarity determining region (CDR) comprising KASQDVGTSVA (SEQ ID NO:20).

57. A complementarity determining region (CDR) comprising WTSTRHT (SEQ ID NO:21).

58. A complementarity determining region (CDR) comprising QQYSLYRS (SEQ ID NO:22).

59. A complementarity determining region (CDR) comprising TYWMS (SEQ ID NO:23).

60. A complementarity determining region (CDR) comprising EIHPDSSTINYAPSLKD (SEQ ID NO:24).

61. A complementarity determining region (CDR) comprising LYFGFPWFAY (SEQ ID NO:25).